ATGGCCCAAGCCCTGCCCTGGCTCCTGCTGTGGATGGCGCGGGAG
TGCTGCCTGCCCACGGCACCCAGCACGGCATCCGGCTGCCCCTGCG
CAGCGGCCTGGGGGGCGCCCCCCTGGGGCTGCGGCTGCCCCGGGA
GACCGACGAAGAGCCCGAGGAGCCCGGCCGGAGGGGCAGCTTTGT
GGAGATGGTGGACAACCTGAGGGGCAAGTCGGGGCAGGGCTACTAC
GTGGAGATGACCGTGGGCAGCCCCCCGCAGACGCTCAACATCCTGG
TGGATACAGGCAGCAGTAACTTTGCAGTGGGTGCTGCCCCCCACCC
CTTCCTGCATCGCTACTACCAGAGGCAGCTGTCCAGCACATACCGGG
ACCTCCGGAAGGGTGTGTATGTGCCCTACACCCAGGGCAAGTGGGA
AGGGGAGCTGGGCACCGACCTGGTAAGCATCCCCCATGGCCCCAAC
GTCACTGTGCGTGCCAACATTGCTGCCATCACTGAATCAGACAAGTT
CTTCATCAACGGCTCCAACTGGGAAGGCATCCTGGGGCTGGCCTATG
CTGAGATTGCCAGGCCTGACGACTCCCTGGAGCCTTTCTTTGACTCT
CTGGTAAAGCAGACCCACGTTCCCAACCTCTTCTCCCTGCAGCTTTG
TGGTGCTGGCTTCCCCCTCAACCAGTCTGAAGTGCTGGCCTCTGTCG
GAGGGAGCATGATCATTGGAGGTATCGACCACTCGCTGTACACAGGC
AGTCTCTGGTATACACCCATCCGGCGGGAGTGGTATTATGAGGTGAT
CATTGTGCGGGTGGAGATCAATGGACAGGATCTGAAAATGGACTGCA
AGGAGTACAACTATGACAAGAGCATTGTGGACAGTGGCACCACCAAC
CTTCGTTTGCCCAAGAAAGTGTTTGAAGCTGCAGTCAAATCCATCAAG
GCAGCCTCCTCCACGGAGAAGTTCCCTGATGGTTTCTGGCTAGGAGA
GCAGCTGGTGTGCTGGCAAGCAGGCACCACCCCTTGGAACATTTTCC
CAGTCATCTCACTCTACCTAATGGGTGAGGTTACCAACCAGTCCTTCC
GCATCACCATCCTTCCGCAGCAATACCTGCGGCCAGTGGAAGATGTG
GCCACGTCCCAAGACGACTGTTACAAGTTTGCCATCTCACAGTCATC
CACGGGCACTGTTATGGGAGCTGTTATCATGGAGGGCTTCTACGTTG
TCTTTGATCGGGCCCGAAAACGAATTGGCTTTGCTGTCAGCGCTTGC
CATGTGCACGATGAGTTCAGGACGGCAGCGGTGGAAGGCCCTTTTG
TCACCTTGGACATGGAAGACTGTGGCTACAACATTCCACAGACAGAT
GAGTCAACCCTCATGACCATAGCCTATGTCATGGCTGCCATCTGCGC
CCTCTTCATGCTGCCACTCTGCCTCATGGTGTGTCAGTGGCGCTGCC
TCCGCTGCCTGCGCCAGCAGCATGATGACTTTGCTGATGACATCTCC
CTGCTGAAG

FIG. 1A

CCATGCCGGCCCCTCACAGCCCCGCCGGGAGCCCGAGCCCGCTGCCCAGG
CTGGCCGCCGCSGTGCCGATGTAGCGGGCTCCGGATCCCAGCCTCTCCCCT
GCTCCCGTGCTCTGCGGATCTCCCCTGACCGCTCTCCACAGCCCGGACCCG
GGGGCTGGCCCAGGGCCCTGCAGGCCCTGGCGTCCTGATGCCCCCAAGCT
CCCTCTCCTGAGAAGCCACCAGCACCACCCAGACTTGGGGGCAGGCGCCA
GGGACGGACGTGGGCCAGTGCGAGCCCAGAGGGCCCGAAGGCCGGGGCC
CACCATGGCCCAAGCCCTGCCCTGGCTCCTGCTGTGGATGGGCGCGGGAG
TGCTGCCTGCCCACGGCACCCAGCACGGCATCCGGCTGCCCCTGCGCAGC
GGCCTGGGGGGCGCCCCCCTGGGGCTGCGGCTGCCCCGGGAGACCGACG
AAGAGCCCGAGGAGCCCGGCCGGAGGGGCAGCTTTGTGGAGATGGTGGAC
AACCTGAGGGGCAAGTCGGGGCAGGGCTACTACGTGGAGATGACCGTGGG
CAGCCCCCCGCAGACGCTCAACATCCTGGTGGATACAGGCAGCAGTAACTT
TGCAGTGGGTGCTGCCCCCCACCCCTTCCTGCATCGCTACTACCAGAGGCA
GCTGTCCAGCACATACCGGGACCTCCGGAAGGGTGTGTATGTGCCCTACAC
CCAGGGCAAGTGGGAAGGGGAGCTGGGCACCGACCTGGTAAGCATCCCCC
ATGGCCCCAACGTCACTGTGCGTGCCAACATTGCTGCCATCACTGAATCAGA
CAAGTTCTTCATCAACGGCTCCAACTGGGAAGGCATCCTGGGGCTGGCCTAT
GCTGAGATTGCCAGGCCTGACGACTCCCTGGAGCCTTTCTTTGACTCTCTGG
TAAAGCAGACCCACGTTCCCAACCTCTTCTCCCTGCAGCTTTGTGGTGCTGG
CTTCCCCCTCAACCAGTCTGAAGTGCTGGCCTCTGTCGGAGGGAGCATGAT
CATTGGAGGTATCGACCACTCGCTGTACACAGGCAGTCTCTGGTATACACCC
ATCCGGCGGGAGTGGTATTATGAGGTGATCATTGTGCGGGTGGAGATCAAT
GGACAGGATCTGAAAATGGACTGCAAGGAGTACAACTATGACAAGAGCATTG
TGGACAGTGGCACCACCAACCTTCGTTTGCCCAAGAAAGTGTTTGAAGCTGC
AGTCAAATCCATCAAGGCAGCCTCCTCCACGGAGAAGTTCCCTGATGGTTTC
TGGCTAGGAGAGCAGCTGGTGTGCTGGCAAGCAGGCACCACCCCTTGGAAC
ATTTTCCCAGTCATCTCACTCTACCTAATGGGTGAGGTTACCAACCAGTCCTT
CCGCATCACCATCCTTCCGCAGCAATACCTGCGGCCAGTGGAAGATGTGGC
CACGTCCCAAGACGACTGTTACAAGTTTGCCATCTCACAGTCATCCACGGGC
ACTGTTATGGGAGCTGTTATCATGGAGGGCTTCTACGTTGTCTTTGATCGGG
CCCGAAAACGAATTGGCTTTGCTGTCAGCGCTTGCCATGTGCACGATGAGTT
CAGGACGGCAGCGGTGGAAGGCCCTTTTGTCACCTTGGACATGGAAGACTG
TGGCTACAACATTCCACAGACAGATGAGTCAACCCTCATGACCATAGCCTAT
GTCATGGCTGCCATCTGCGCCCTCTTCATGCTGCCACTCTGCCTCATGGTGT
GTCAGTGGCGCTGCCTCCGCTGCCTGCGCCAGCAGCATGATGACTTTGCTG
ATGACATCTCCCTGCTGAAGTGAGGAGGCCCATGGGCAGAAGATAGAGATT
CCCCTGGACCACACCTCCGTGGTTCACTTTGGTCACAAGTAGGAGACACAGA
TGGCACCTGTGGCCAGAGCACCTCAGGACCCTCCCCACCCACCAAATGCCT
CTGCCTTGATGGAGAAGGAAAAGGCTGGCAAGGTGGGTTCCAGGGACTGTA
CCTGTAGGAAACAGAAAAGAGAAGAAAGAAGCACTCTGCTGGCGGGAATAC
TCTTGGTCACCTCAAATTTAAGTCGGGAAATTCTGCTGCTTGAAACTTCAGCC
CTGAACCTTTGTCCACCATTCCTTTAAATTCTCCAACCCAAAGTATTCTTCTTT
TCTTAGTTTCAGAAGTACTGGCATCACACGCAGGTTACCTTGGCGTGTGTCC
CTGTGGTACCCTGGCAGAGAAGAGACCAAGCTTGTTTCCCTGCTGGCCAAA
GTCAGTAGGAGAGGATGCACAGTTTGCTATTTGCTTTAGAGACAGGGACTGT
ATAAACAAGCCTAACATTGGTGCAAAGATTGCCTCTTGAATT

FIG. 1B

MAQALPWLLLWMGAGVLPAHGTQHGIRLPLRSGLGGAPLGLRL
PRETDEEPEEPGRRGSFVEMVDNLRGKSGQGYYVEMTVGSPP
QTLNILVDTGSSNFAVGAAPHPFLHRYYQRQLSSTYRDLRKGVY
VPYTQGKWEGELGTDLVSIPHGPNVTVRANIAAITESDKFFINGS
NWEGILGLAYAEIARPDDSLEPFFDSLVKQTHVPNLFSLQLCGAG
FPLNQSEVLASVGGSMIIGGIDHSLYTGSLWYTPIRREWYYEVIIV
RVEINGQDLKMDCKEYNYDKSIVDSGTTNLRLPKKVFEAAVKSIK
AASSTEKFPDGFWLGEQLVCWQAGTTPWNIFPVISLYLMGEVTN
QSFRITILPQQYLRPVEDVATSQDDCYKFAISQSSTGTVMGAVIM
EGFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTLDMEDC
GYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWRCLRCLR
QQHDDFADDISLLK

FIG. 2A

ETDEEPEEPGRRGSFVEMVDNLRGKSGQGYYVEMTVGSPPQT
LNILVDTGSSNFAVGAAPHPFLHRYYQRQLSSTYRDLRKGVYVP
YTQGKWEGELGTDLVSIPHGPNVTVRANIAAITESDKFFINGSNW
EGILGLAYAEIARPDDSLEPFFDSLVKQTHVPNLFSLQLCGAGFP
LNQSEVLASVGGSMIIGGIDHSLYTGSLWYTPIRREWYYEVIIVRV
EINGQDLKMDCKEYNYDKSIVDSGTTNLRLPKKVFEAAVKSIKAA
SSTEKFPDGFWLGEQLVCWQAGTTPWNIFPVISLYLMGEVTNQ
SFRITILPQQYLRPVEDVATSQDDCYKFAISQSSTGTVMGAVIME
GFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTLDMEDC
GYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWRCLRCLR
QQHDDFADDISLLK

FIG. 2B

MAQALPWLLLWMGAGVLPAHGTQHGIRLPLRSGLGGAPLGLRL
PRETDEEPEEPGRRGSFVEMVDNLRGKSGQGYYVEMTVGSPP
QTLNILVDTGSSNFAVGAAPHPFLHRYYQRQLSSTYRDLRKGVY
VPYTQGKWEGELGTDLVSIPHGPNVTVRANIAAITESDKFFINGS
NWEGILGLAYAEIARPDDSLEPFFDSLVKQTHVPNLFSLQLCGAG
FPLNQSEVLASVGGSMIIGGIDHSLYTGSLWYTPIRREWYYEVIIV
RVEINGQDLKMDCKEYNYDKSIVDSGTTNLRLPKKVFEAAVKSIK
AASSTEKFPDGFWLGEQLVCWQAGTTPWNIFPVISLYLMGEVTN
QSFRITILPQQYLRPVEDVATSQDDCYKFAISQSSTGTVMGAVIM
EGFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTLDMEDC
GYNIPQTDE<u>DYKDDDDK</u>

FIG. 3A

ETDEEPEEPGRRGSFVEMVDNLRGKSGQGYYVEMTVGSPPQT
LNILVDTGSSNFAVGAAPHPFLHRYYQRQLSSTYRDLRKGVYVP
YTQGKWEGELGTDLVSIPHGPNVTVRANIAAITESDKFFINGSNW
EGILGLAYAEIARPDDSLEPFFDSLVKQTHVPNLFSLQLCGAGFP
LNQSEVLASVGGSMIIGGIDHSLYTGSLWYTPIRREWYYEVIIVRV
EINGQDLKMDCKEYNYDKSIVDSGTTNLRLPKKVFEAAVKSIKAA
SSTEKFPDGFWLGEQLVCWQAGTTPWNIFPVISLYLMGEVTNQ
SFRITILPQQYLRPVEDVATSQDDCYKFAISQSSTGTVMGAVIME
GFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTLDMEDC
GYNIPQTDE<u>DYKDDDDK</u>

FIG. 3B

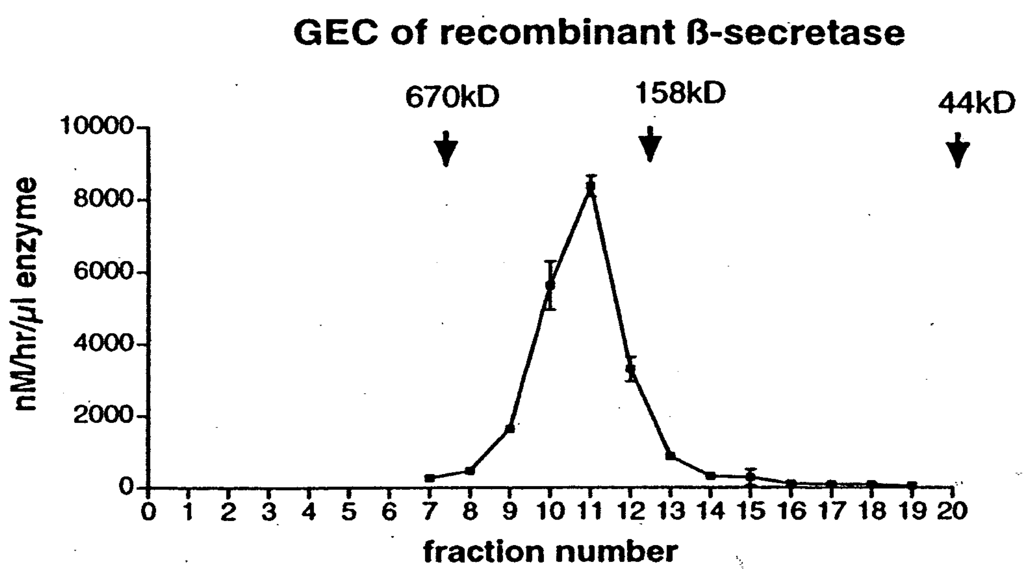

GEC of recombinant ß-secretase
670kD
158kD
44kD
nM/hr/µl enzyme
10000
8000
6000
4000
2000
0
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
fraction number

FIG. 4

Fig. 5A

```
atg gcc caa gcc ctg ccc tgg ctc ctg ctg tgg atg ggc gcg gga gtg    48
Met Ala Gln Ala Leu Pro Trp Leu Leu Leu Trp Met Gly Ala Gly Val
  1               5                  10                  15
[                        Signal peptide                        ]

ctg cct gcc cac ggc acc cag cac ggc atc cgg ctg ccc ctg cgc agc    96
Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser
             20                  25                  30
[  Signal peptide  >[               pro region                 ]

ggc ctg ggg ggc gcc ccc ctg ggg ctg cgg ctg ccc cgg gag acc gac   144
Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp
         35                  40                  45
[                 pro region                 >[  N term seq   ]

gaa gag ccc gag gag ccc ggc cgg agg ggc agc ttt gtg gag atg gtg   192
Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val
     50                  55                  60
[                    N terminal sequence                       ]

gac aac ctg agg ggc aag tcg ggg cag ggc tac tac gtg gag atg acc   240
Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr
 65                  70                  75                  80
[N terminal sequence]

gtg ggc agc ccc ccg cag acg ctc aac atc ctg gtg gat aca ggc agc   288
Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser
                 85                  90                  95
                                                <  Active-D  >

agt aac ttt gca gtg ggt gct gcc ccc cac ccc ttc ctg cat cgc tac   336
Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr
            100                 105                 110
```

Fig. 5B

```
tac cag agg cag ctg tcc agc aca tac cgg gac ctc cgg aag ggt gtg   384
Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val
        115                 120                 125

tat gtg ccc tac acc cag ggc aag tgg gaa ggg gag ctg ggc acc gac   432
Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp
    130                 135                 140

ctg gta agc atc ccc cat ggc ccc aac gtc act gtg cgt gcc aac att   480
Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile
145                 150                 155                 160
                                [N-glycos  ]

gct gcc atc act gaa tca gac aag ttc ttc atc aac ggc tcc aac tgg   528
Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp
                165                 170                 175
                                            [N-glycos  ]
gaa ggc atc ctg ggg ctg gcc tat gct gag att gcc agg cct gac gac   576
Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp
            180                 185                 190

tcc ctg gag cct ttc ttt gac tct ctg gta aag cag acc cac gtt ccc   624
Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro
        195                 200                 205

aac ctc ttc tcc ctg cag ctt tgt ggt gct ggc ttc ccc ctc aac cag   672
Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln
    210                 215                 220
                                                        [N-glycos]
```

Fig. 5C

```
tct gaa gtg ctg gcc tct gtc gga ggg agc atg atc att gga ggt atc   720
Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile
225                 230                 235                 240
N-gly

gac cac tcg ctg tac aca ggc agt ctc tgg tat aca ccc atc cgg cgg   768
Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg
                245                 250                 255

gag tgg tat tat gag gtg atc att gtg cgg gtg gag atc aat gga cag   816
Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln
            260                 265                 270

gat ctg aaa atg gac tgc aag gag tac aac tat gac aag agc att gtg   864
Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val
        275                 280                 285

gac agt ggc acc acc aac ctt cgt ttg ccc aag aaa gtg ttt gaa gct   912
Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala
    290                 295                 300
  Active-D
gca gtc aaa tcc atc aag gca gcc tcc tcc acg gag aag ttc cct gat   960
Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp
305                 310                 315                 320

ggt ttc tgg cta gga gag cag ctg gtg tgc tgg caa gca ggc acc acc   1008
Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr
                325                 330                 335
```

Fig. 5D

```
cct tgg aac att ttc cca gtc atc tca ctc tac cta atg ggt gag gtt   1056
Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val
            340                 345                 350

acc aac cag tcc ttc cgc atc acc atc ctt ccg cag caa tac ctg cgg   1104
Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg
        355                 360                 365

    N-glycos
cca gtg gaa gat gtg gcc acg tcc caa gac gac tgt tac aag ttt gcc   1152
Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala
    370                 375                 380

atc tca cag tca tcc acg ggc act gtt atg gga gct gtt atc atg gag   1200
Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu
385                 390                 395                 400

ggc ttc tac gtt gtc ttt gat cgg gcc cga aaa cga att ggc ttt gct   1248
Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala
                405                 410                 415

gtc agc gct tgc cat gtg cac gat gag ttc agg acg gca gcg gtg gaa   1296
Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu
            420                 425                 430
Internal peptide sequence
```

Fig. 5E

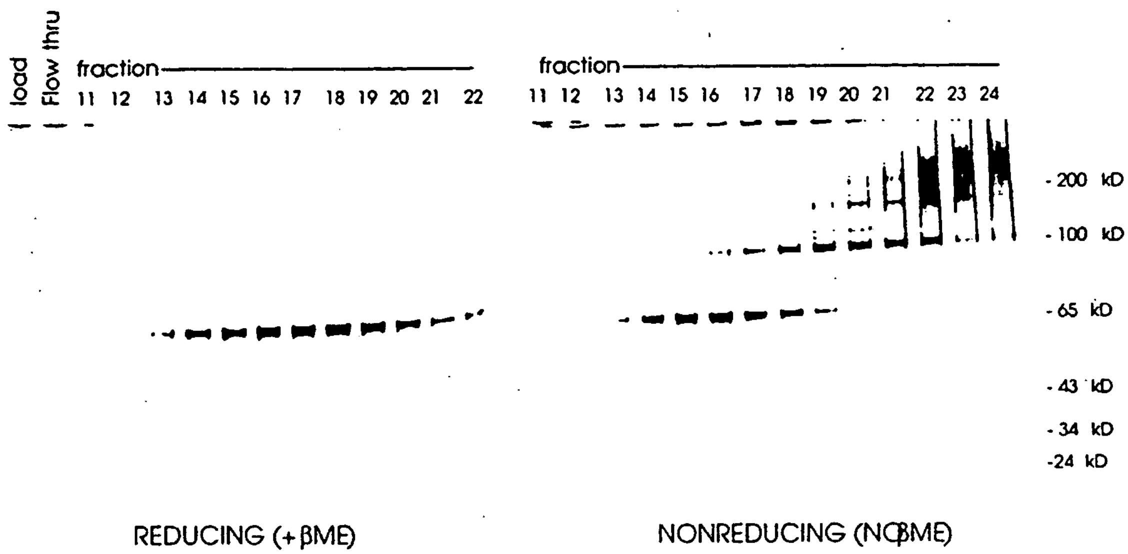
```
ggc cct ttt gtc acc ttg gac atg gaa gac tgt ggc tac aac att cca   1344
Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro
        435                 440                 445

cag aca gat gag tca acc ctc atg acc ata gcc tat gtc atg gct gcc   1392
Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met Ala Ala
    450                 455                 460

                        [          Transmembrane              ]
atc tgc gcc ctc ttc atg ctg cca ctc tgc ctc atg gtg tgt cag tgg   1440
Ile Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val Cys Gln Trp
465                 470                 475                 480
[                     Transmembrane                           ]

cgc tgc ctc cgc tgc ctg cgc cag cag cat gat gac ttt gct gat gac   1488
Arg Cys Leu Arg Cys Leu Arg Gln Gln His Asp Asp Phe Ala Asp Asp
            485                 490                 495

atc tcc ctg ctg aag tga                                           1506
Ile Ser Leu Leu Lys
        500
```



load
Flow thru
fraction
11 12 13 14 15 16 17 18 19 20 21 22
fraction
11 12 13 14 15 16 17 18 19 20 21 22 23 24
-200 kD
-100 kD
-65 kD
-43 kD
-34 kD
-24 kD
REDUCING (+βME)
NONREDUCING (NOβME)

FIG. 6A

FIG. 6B

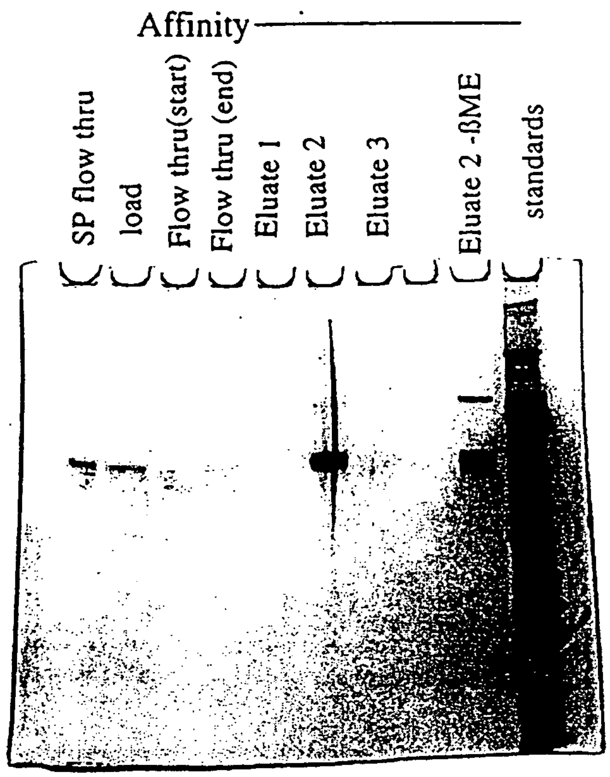

Affinity
SP flow thru
load
Flow thru(start)
Flow thru (end)
Eluate 1
Eluate 2
Eluate 3
Eluate 2 -ßME
standards

FIG. 7

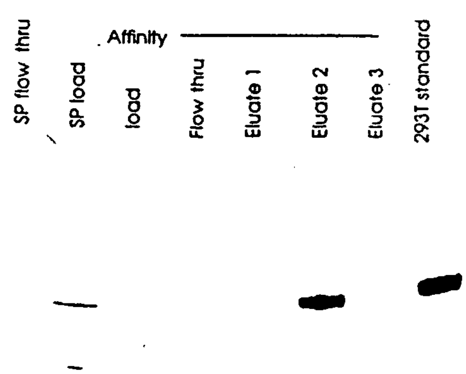

Affinity
SP flow thru
SP load
load
Flow thru
Eluate 1
Eluate 2
Eluate 3
293T standard

FIG. 8

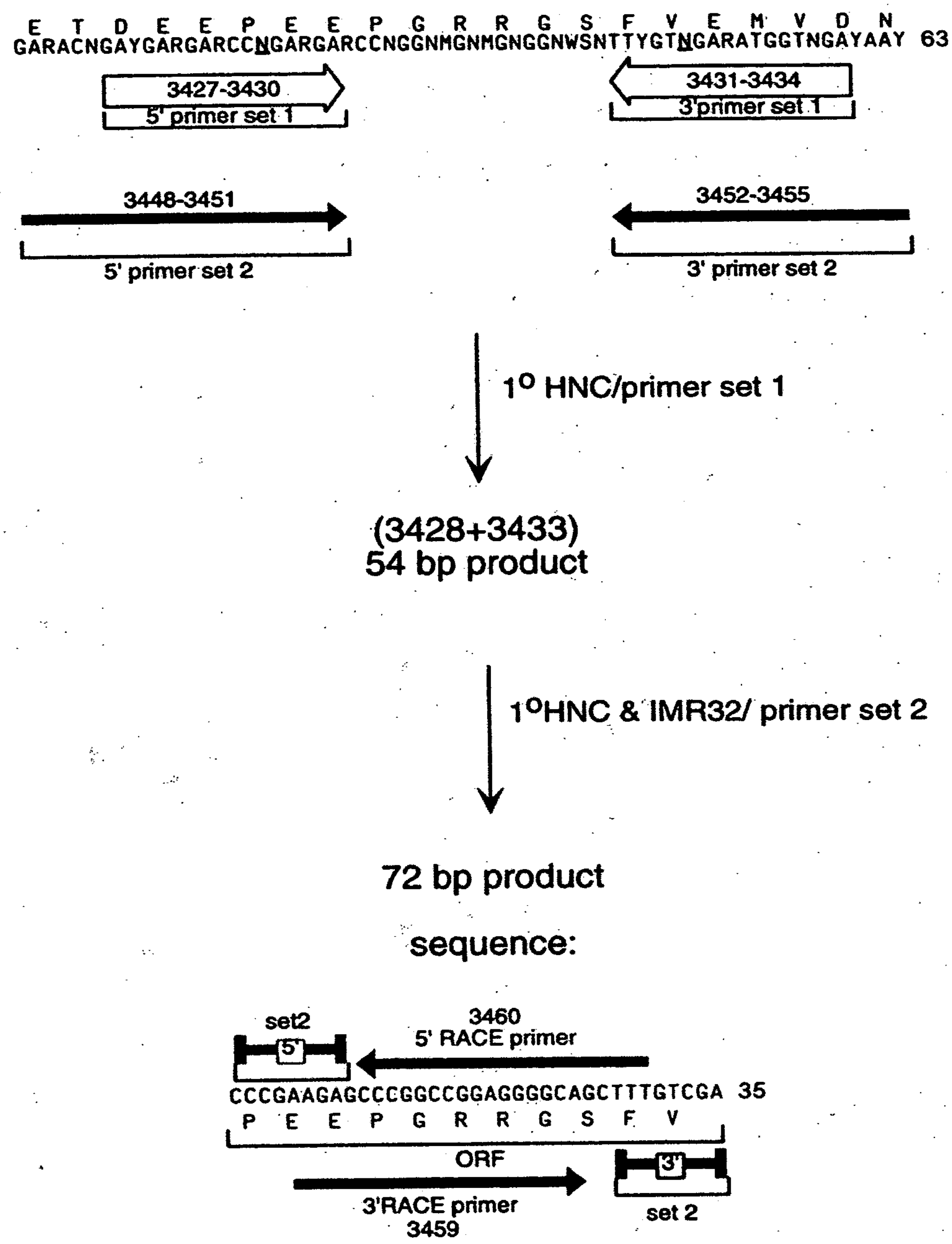

E T D E E P E E P G R R G S F V E M V D N
GARACNGAYGARGARCCNGARGARCCNGGNMGNMGNGGNWSNTTYGTNGARATGGTNGAYAAY 63
3427-3430
5' primer set 1
3431-3434
3'primer set 1
3448-3451
5' primer set 2
3452-3455
3' primer set 2
1° HNC/primer set 1
(3428+3433)
54 bp product
1°HNC & IMR32/ primer set 2
72 bp product
sequence:
set2
5'
3460
5' RACE primer
CCCGAAGAGCCCGGCCGGAGGGGCAGCTTTGTCGA 35
P E E P G R R G S F V
ORF
3'
set 2
3'RACE primer
3459

Fig. 9

```
                        10        20        30        40
Hump501prot  MAQALPWLLLWMGAGVLPAHGTQHGIRLPLRSGLGGAPLG   40
Musp501prot  MAPALHWLLLWVGSGMLPAQGTHLGIRLPLRSGLAGPPLG   40

                        50        60        70        80
Hump501prot  LRLPRETDEEPEEPGRRGSFVEMVDNLRGKSGQGYYVEMT   80
Musp501prot  LRLPRETDEESEEPGRRGSFVEMVDNLRGKSGQGYYVEMT   80

                        90       100       110       120
Hump501prot  VGSPPQTLNILVDTGSSNFAVGAAPHPFLHRYYQRQLSST  120
Musp501prot  VGSPPQTLNILVDTGSSNFAVGAAPHPFLHRYYQRQLSST  120

                       130       140       150       160
Hump501prot  YRDLRKGVYVPYTQGKWEGELGTDLVSIPHGPNVTVRANI  160
Musp501prot  YRDLRKGVYVPYTQGKWEGELGTDLVSIPHGPNVTVRANI  160

                       170       180       190       200
Hump501prot  AAITESDKFFINGSNWEGILGLAYAEIARPDDSLEPFFDS  200
Musp501prot  AAITESDKFFINGSNWEGILGLAYAEIARPDDSLEPFFDS  200

                       210       220       230       240
Hump501prot  LVKQTHVPNLFSLQLCGAGFPLNQSEVLASVGGSMIIGGI  240
Musp501prot  LVKQTHIPNIFSLQLCGAGFPLNQTEALASVGGSMIIGGI  240

                       250       260       270       280
Hump501prot  DHSLYTGSLWYTPIRREWYYEVIIVRVEINGQDLKMDCKE  280
Musp501prot  DHSLYTGSLWYTPIRREWYYEVIIVRVEINGQDLKMDCKE  280

                       290       300       310       320
Hump501prot  YNYDKSIVDSGTTNLRLPKKVFEAAVKSIKAASSTEKFPD  320
Musp501prot  YNYDKSIVDSGTTNLRLPKKVFEAAVKSIKAASSTEKFPD  320

                       330       340       350       360
Hump501prot  GFWLGEQLVCWQAGTTPWNIFPVISLYLMGEVTNQSFRIT  360
Musp501prot  GFWLGEQLVCWQAGTTPWNIFPVISLYLMGEVTNQSFRIT  360

                       370       380       390       400
Hump501prot  ILPQQYLRPVEDVATSQDDCYKFAISQSSTGTVMGAVIME  400
Musp501prot  ILPQQYLRPVEDVATSQDDCYKFAVSQSSTGTVMGAVIME  400

                       410       420       430       440
Hump501prot  GFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTLDM  440
Musp501prot  GFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTADM  440

                       450       460       470       480
Hump501prot  EDCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQW  480
Musp501prot  EDCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQW  480

                       490       500
Hump501prot  RCLRCLRQQHDDFADDISLLK                     501
Musp501prot  RCLRCLRHQHDDFGDDISLLK                     501
```

FIG. 10

CTGTTGGGCTCGCGGTTGAGGACAAACTCTTCGCGGTCTTTCCAGTACTCT
TGGATCGGAAACCCGTCGGCCTCCGAACGGTACTCCGCCACCGAGGGACCT
GAGCGAGTCCGCATCGACCGGATCGGAAAACCTCTCGACTGTTGGGGTGAG
TACTCCCTCTCAAAAGCGGGCATGACTTCTGCGCTAAGATTGTCAGTTTCC
AAAAACGAGGAGGATTTGATATTCACCTGGCCCGCGGTGATGCCTTTGAGG
GTGGCCGCGTCCATCTGGTCAGAAAAGACAATCTTTTTGTTGTCAAGCTTG
AGGTGTGGCAGGCTTGAGATCTGGCCATACACTTGAGTGACAATGACATCC
ACTTTGCCTTTCTCTCCACAGGTGTCCACTCCCAGGTCCAACTGCAGGTCG
ACTCTAGACCC

FIG. 11A

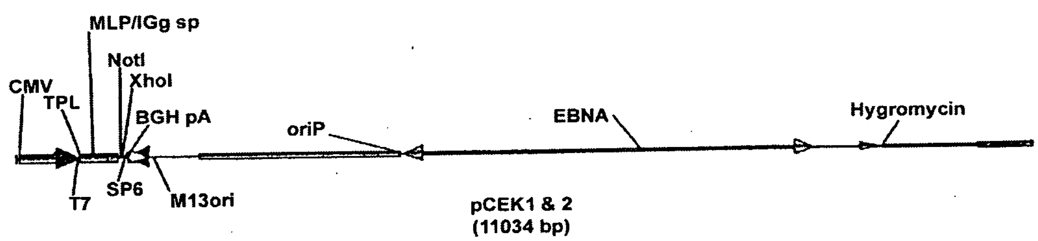


FIG. 11B

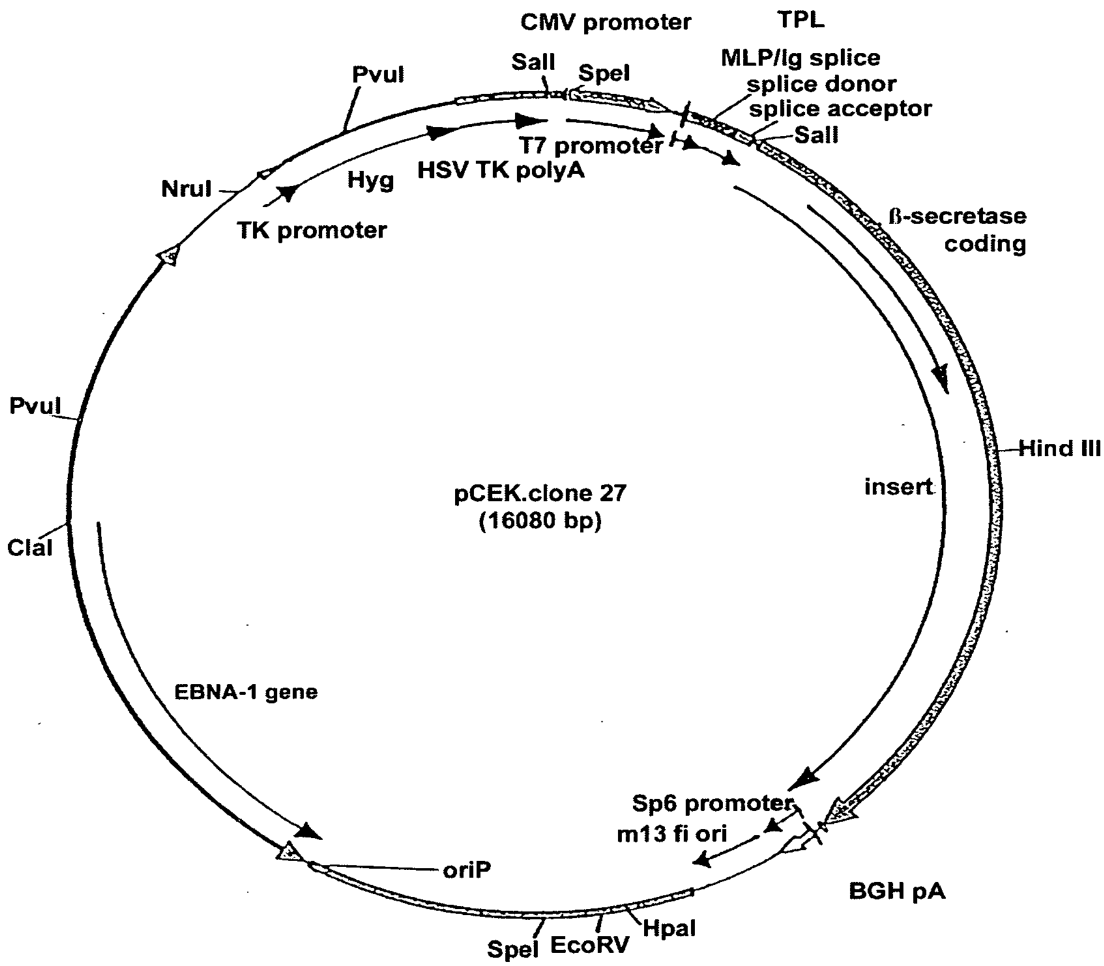

CMV promoter
TPL
SalI
SpeI
MLP/Ig splice
splice donor
splice acceptor
SalI
PvuI
T7 promoter
HSV TK polyA
Hyg
NruI
TK promoter
ß-secretase
coding
PvuI
Hind III
pCEK.clone 27
(16080 bp)
insert
ClaI
EBNA-1 gene
Sp6 promoter
m13 fi ori
oriP
BGH pA
HpaI
SpeI
EcoRV

FIG. 12

Figure 13A

```
ttctcatgtt tgacagctta tcatcgcaga tccgggcaac gttgttgcat tgctgcaggc 60

gcagaactgg taggtatgga agatccgatg tacgggccag atatacgcgt tgacattgat 120
     SpeI
tattgactag ttattaatag taatcaatta cggggtcatt agttcatagc ccatatatgg 180

agttccgcgt tacataactt acggtaaatg gcccgcctgg ctgaccgccc aacgaccccc 240

gcccattgac gtcaataatg acgtatgttc ccatagtaac gccaataggg actttccatt 300

gacgtcaatg ggtggactat ttacggtaaa ctgcccactt ggcagtacat caagtgtatc 360

atatgccaag tacgccccct attgacgtca atgacggtaa atggcccgcc tggcattatg 420

cccagtacat gaccttatgg gactttccta cttggcagta catctacgta ttagtcatcg 480

ctattaccat ggtgatgcgg ttttggcagt acatcaatgg gcgtggatag cggtttgact 540

cacggggatt tccaagtctc caccccattg acgtcaatgg gagtttgttt tggcaccaaa 600

atcaacggga ctttccaaaa tgtcgtaaca actccgcccc attgacgcaa atgggcggta 660

ggcgtgtacg gtgggaggtc tatataagca gagctctctg gctaactaga gaacccactg 720

cttactggct tatcgaaatt aatacgactc actataggga gacccaagct ctgttgggct 780
```

Figure 13B

cgcggttgag gacaaactct tcgcggtctt tccagtactc ttggatcgga aacccgtcgg 840

cctccgaacg gtactccgcc accgagggac ctgagcgagt ccgcatcgac cggatcggaa 900

splice donor

aacctctcga ctgttggggt gagtactccc tctcaaaagc gggcatgact tctgcgctaa 960

gattgtcagt ttccaaaaac gaggaggatt tgatattcac ctggcccgcg gtgatgcctt 1020

tgagggtggc cgcgtccatc tggtcagaaa agacaatctt tttgttgtca agcttgaggt 1080

gtggcaggct tgagatctgg ccatacactt gagtgacaat gacatccact ttgcctttct 1140

splice acceptor SalI

ctccacaggt gtccactccc aggtccaact gcaggtcgac tctagacccg gggaattctg 1200

cagatatcca tcacactggc cgcactcgtc cccagcccgc ccgggagctg cgagccgcga 1260

gctggattat ggtggcctga gcagccaacg cagccgcagg agcccggagc ccttgcccct 1320

gcccgcgccg ccgcccgccg gggggaccag ggaagccgcc accggcccgc catgcccgcc 1380

cctcccagcc ccgccgggag cccgcgcccg ctgcccaggc tggccgccgc cgtgccgatg 1440

tagcgggctc cggatcccag cctctcccct gctcccgtgc tctgcggatc tcccctgacc 1500

gctctccaca gcccggaccc gggggctggc ccagggccct gcaggccctg gcgtcctgat 1560

gcccccaagc tccctctcct gagaagccac cagcaccacc cagacttggg ggcaggcgcc 1620

Figure 13C

```
agggacggac gtgggccagt gcgagcccag agggcccgaa ggccggggcc cacc atg    1677
                                                            Met
                                                              1

gcc caa gcc ctg ccc tgg ctc ctg ctg tgg atg ggc gcg gga gtg ctg    1725
Ala Gln Ala Leu Pro Trp Leu Leu Leu Trp Met Gly Ala Gly Val Leu
                  5                  10                  15

cct gcc cac ggc acc cag cac ggc atc cgg ctg ccc ctg cgc agc ggc    1773
Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser Gly
             20                  25                  30

ctg ggg ggc gcc ccc ctg ggg ctg cgg ctg ccc cgg gag acc gac gaa    1821
Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp Glu
         35                  40                  45

gag ccc gag gag ccc ggc cgg agg ggc agc ttt gtg gag atg gtg gac    1869
Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val Asp
 50                  55                  60                  65

aac ctg agg ggc aag tcg ggg cag ggc tac tac gtg gag atg acc gtg    1917
Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr Val
                 70                  75                  80

ggc agc ccc ccg cag acg ctc aac atc ctg gtg gat aca ggc agc agt    1965
Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser Ser
                 85                  90                  95
```

Figure 13D

```
aac ttt gca gtg ggt gct gcc ccc cac ccc ttc ctg cat cgc tac tac    2013
Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr Tyr
        100                 105                 110

cag agg cag ctg tcc agc aca tac cgg gac ctc cgg aag ggt gtg tat    2061
Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val Tyr
    115                 120                 125

gtg ccc tac acc cag ggc aag tgg gaa ggg gag ctg ggc acc gac ctg    2109
Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp Leu
130                 135                 140                 145

gta agc atc ccc cat ggc ccc aac gtc act gtg cgt gcc aac att gct    2157
Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile Ala
                150                 155                 160

gcc atc act gaa tca gac aag ttc ttc atc aac ggc tcc aac tgg gaa    2205
Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp Glu
            165                 170                 175

ggc atc ctg ggg ctg gcc tat gct gag att gcc agg cct gac gac tcc    2253
Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp Ser
        180                 185                 190

ctg gag cct ttc ttt gac tct ctg gta aag cag acc cac gtt ccc aac    2301
Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro Asn
    195                 200                 205
```

Figure 13E

```
ctc ttc tcc ctg cag ctt tgt ggt gct ggc ttc ccc ctc aac cag tct    2349
Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln Ser
210                 215                 220                 225

gaa gtg ctg gcc tct gtc gga ggg agc atg atc att gga ggt atc gac    2397
Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile Asp
                230                 235                 240

cac tcg ctg tac aca ggc agt ctc tgg tat aca ccc atc cgg cgg gag    2445
His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg Glu
            245                 250                 255

tgg tat tat gag gtc atc att gtg cgg gtg gag atc aat gga cag gat    2493
Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln Asp
        260                 265                 270

ctg aaa atg gac tgc aag gag tac aac tat gac aag agc att gtg gac    2541
Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val Asp
    275                 280                 285

agt ggc acc acc aac ctt cgt ttg ccc aag aaa gtg ttt gaa gct gca    2589
Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala Ala
290                 295                 300                 305

gtc aaa tcc atc aag gca gcc tcc tcc acg gag aag ttc cct gat ggt    2637
Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp Gly
                310                 315                 320
```

Figure 13F

```
ttc tgg cta gga gag cag ctg gtg tgc tgg caa gca ggc acc acc cct     2685
Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr Pro
            325                 330                 335

tgg aac att ttc cca gtc atc tca ctc tac cta atg ggt gag gtt acc     2733
Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val Thr
        340                 345                 350

aac cag tcc ttc cgc atc acc atc ctt ccg cag caa tac ctg cgg cca     2781
Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg Pro
    355                 360                 365

gtg gaa gat gtg gcc acg tcc caa gac gac tgt tac aag ttt gcc atc     2829
Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala Ile
370                 375                 380                 385

tca cag tca tcc acg ggc act gtt atg gga gct gtt atc atg gag ggc     2877
Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu Gly
                390                 395                 400

ttc tac gtt gtc ttt gat cgg gcc cga aaa cga att ggc ttt gct gtc     2925
Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala Val
            405                 410                 415

agc gct tgc cat gtg cac gat gag ttc agg acg gca gcg gtg gaa ggc     2973
Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu Gly
        420                 425                 430
```

Figure 13G

```
cct ttt gtc acc ttg gac atg gaa gac tgt ggc tac aac att cca cag   3021
Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro Gln
    435                 440                 445

aca gat gag tca acc ctc atg acc ata gcc tat gtc atg gct gcc atc   3069
Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met Ala Ala Ile
450                 455                 460                 465

tgc gcc ctc ttc atg ctg cca ctc tgc ctc atg gtg tgt cag tgg cgc   3117
Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val Cys Gln Trp Arg
                470                 475                 480

tgc ctc cgc tgc ctg cgc cag cag cat gat gac ttt gct gat gac atc   3165
Cys Leu Arg Cys Leu Arg Gln Gln His Asp Asp Phe Ala Asp Asp Ile
            485                 490                 495

tcc ctg ctg aag tga ggaggcccat gggcagaaga tagagattcc cctggaccac   3220
Ser Leu Leu Lys
        500

acctccgtgg ttcactttgg tcacaagtag gagacacaga tggcacctgt ggccagagca 3280

cctcaggacc ctccccaccc accaaatgcc tctgccttga tggagaagga aaaggctggc 3340

aaggtgggtt ccagggactg tacctgtagg aaacagaaaa gagaagaaag aagcactctg 3400

ctggcgggaa tactcttggt cacctcaaat ttaagtcggg aaattctgct gcttgaaact 3460
```

Figure 13H

tcagccctga acctttgtcc accattcctt taaattctcc aacccaaagt attcttcttt 3520

tcttagtttc agaagtactg gcatcacacg caggttacct tggcgtgtgt ccctgtggta 3580

HindIII

ccctggcaga gaagagacca agcttgtttc cctgctggcc aaagtcagta ggagaggatg 3640

cacagtttgc tatttgcttt agagacaggg actgtataaa caagcctaac attggtgcaa 3700

agattgcctc ttgaattaaa aaaaaaaact agattgacta tttatacaaa tgggggcggc 3760

tggaaagagg agaaggagag ggagtacaaa gacagggaat agtgggatca aagctaggaa 3820

aggcagaaac acaaccactc accagtccta gttttagacc tcatctccaa gatagcatcc 3880

catctcagaa gatgggtgtt gttttcaatg ttttcttttc tgtggttgca gcctgaccaa 3940

aagtgagatg ggaagggctt atctagccaa agagctcttt tttagctctc ttaaatgaag 4000

tgcccactaa gaagttccac ttaacacatg aatttctgcc atattaattt cattgtctct 4060

atctgaacca ccctttattc tacatatgat aggcagcact gaaatatcct aaccccctaa 4120

gctccaggtg ccctgtggga gagcaactgg actatagcag ggctgggctc tgtcttcctg 4180

gtcataggct cactctttcc cccaaatctt cctctggagc tttgcagcca aggtgctaaa 4240

aggaataggt aggagacctc ttctatctaa tccttaaaag cataatgttg aacattcatt 4300

Figure 13I

caacagctga tgccctataa cccctgcctg gatttcttcc tattaggcta taagaagtag 4360

caagatcttt acataattca gagtggtttc attgccttcc taccctctct aatggcccct 4420

ccatttattt gactaaagca tcacacagtg gcactagcat tataccaaga gtatgagaaa 4480

tacagtgctt tatggctcta acattactgc cttcagtatc aaggctgcct ggagaaagga 4540

tggcagcctc agggcttcct tatgtcctcc accacaagag ctccttgatg aaggtcatct 4600

ttttccccta tcctgttctt cccctccccg ctcctaatgg tacgtgggta cccaggctgg 4660

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actacggtac cagtgttagt gggaagagct gggttttcct agtataccca ctgcatccta 4780

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caagccataa accaataaaa caagaatact gagtcagttt tttatctggg ttctcttcat 4960

tcccactgca cttggtgctg ctttggctga ctgggaacac cccataacta cagagtctga 5020

caggaagact ggagactgtc cacttctagc tcggaactta ctgtgtaaat aaactttcag 5080

aactgctacc atgaagtgaa aatgccacat tttgctttat aatttctacc catgttggga 5140

Figure 13J

aaaactggct ttttcccagc cctttccagg gcataaaact caaccccttc gatagcaagt 5200

cccatcagcc tattattttt ttaaagaaaa cttgcacttg tttttctttt tacagttact 5260

tccttcctgc cccaaaatta taaactctaa gtgtaaaaaa aagtcttaac aacagcttct 5320

tgcttgtaaa aatatgtatt atacatctgt atttttaaat tctgctcctg aaaaatgact 5380

gtcccattct ccactcactg catttggggc ctttcccatt ggtctgcatg tcttttatca 5440

ttgcaggcca gtggacagag ggagaaggga gaacaggggt cgccaacact tgtgttgctt 5500

tctgactgat cctgaacaag aaagagtaac actgaggcgc tcgctcccat gcacaactct 5560

ccaaaacact tatcctcctg caagagtggg ctttccgggt ctttactggg aagcagttaa 5620

gccccctcct caccccttcc ttttttcttt ctttactcct ttggcttcaa aggattttgg 5680

aaaagaaaca atatgcttta cactcatttt caatttctaa atttgcaggg gatactgaaa 5740

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aagataaaaa acgaatcccc taaacaaaaa gaacaataga actggtcttc cattttgcca 5860

cctttcctgt tcatgacagc tactaacctg gagacagtaa catttcatta accaaagaaa 5920

gtgggtcacc tgacctctga agagctgagt actcaggcca ctccaatcac cctacaagat 5980

Figure 13K

gccaaggagg tcccaggaag tccagctcct taaactgacg ctagtcaata aacctgggca 6040

agtgaggcaa gagaaatgag gaagaatcca tctgtgaggt gacaggcacg gatgaaagac 6100

aaagacggaa aagagtatca aaggcagaaa ggagatcatt tagttgggtc tgaaaggaaa 6160

agtntttgct atccgacatg tactgctagt wcctgtaagc attttaggtc ccagaatgga 6220

aaaaaaaatc aagctatngg ttatataata atgnnnnnnn nnnnnnnnnn nntcgagcat 6280

gcatctagag ggccctattc tatagtgtca cctaaatgct agagctcgct gatcagcctc 6340

gactgtgcct tctagttgcc agccatctgt tgtttgcccc tcccccgtgc cttccttgac 6400

cctggaaggt gccactccca ctgtcctttc ctaataaaat gaggaaattg catcgcattg 6460

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ggcgggtgtg gtggttacgc gcagcgtgac cgctacactt gccagcgccc tagcgcccgc 6700

tcctttcgct ttcttccctt cctttctcgc cacgttcgcc ggctttcccc gtcaagctct 6760

aaatcggggc atccctttag ggttccgatt tagtgcttta cggcacctcg accccaaaaa 6820

Figure 13L

```
acttgattag ggtgatggtt cacgtagtgg gccatcgccc tgatagacgg tttttcgccc 6880

tttgacgttg gagtccacgt tctttaatag tggactcttg ttccaaactg gaacaacact 6940

caaccctatc tcggtctatt cttttgattt ataagggatt ttggggattt cggcctattg 7000

gttaaaaaat gagctgattt aacaaaaatt taacgcgaat tctagagccc cgccgccgga 7060

cgaactaaac ctgactacgg catctctgcc ccttcttcgc ggggcagtgc atgtaatccc 7120

ttcagttggt tggtacaact tgccaactgg gccctgttcc acatgtgaca cggggggga 7180

ccaaacacaa aggggttctc tgactgtagt tgacatcctt ataaatggat gtgcacattt 7240

gccaacactg agtggctttc atcctggagc agactttgca gtctgtggac tgcaacacaa 7300

cattgccttt atgtgtaact cttggctgaa gctcttacac caatgctggg ggacatgtac 7360

ctcccagggg cccaggaaga ctacgggagg ctacaccaac gtcaatcaga ggggcctgtg 7420

tagctaccga taagcggacc ctcaagaggg cattagcaat agtgtttata aggcccctt 7480
HpaI
gttaacccta aacgggtagc atatgcttcc cgggtagtag tatatactat ccagactaac 7540

cctaattcaa tagcatatgt tacccaacgg gaagcatatg ctatcgaatt agggttagta 7600
                      EcoRV
aaagggtcct aaggaacagc gatatctccc accccatgag ctgtcacggt tttatttaca 7660
```

Figure 13M

```
tggggtcagg attccacgag ggtagtgaac cattttagtc acaagggcag tggctgaaga 7720

tcaaggagcg ggcagtgaac tctcctgaat cttcgcctgc ttcttcattc tccttcgttt 7780

agctaataga ataactgctg agttgtgaac agtaaggtgt atgtgaggtg ctcgaaaaca 7840

aggtttcagg tgacgccccc agaataaaat ttggacgggg ggttcagtgg tggcattgtg 7900
                                                 SpeI
ctatgacacc aatataaccc tcacaaaccc cttgggcaat aaatactagt gtaggaatga 7960

aacattctga atatctttaa caatagaaat ccatggggtg gggacaagcc gtaaagactg 8020

gatgtccatc tcacacgaat ttatggctat gggcaacaca taatcctagt gcaatatgat 8080

actggggtta ttaagatgtg tcccaggcag ggaccaagac aggtgaacca tgttgttaca 8140

ctctatttgt aacaagggga aagagagtgg acgccgacag cagcggactc cactggttgt 8200

ctctaacacc cccgaaaatt aaacggggct ccacgccaat ggggcccata aacaaagaca 8260

agtggccact cttttttttg aaattgtgga gtgggggcac gcgtcagccc ccacacgccg 8320

ccctgcggtt ttggactgta aaataagggt gtaataactt ggctgattgt aaccccgcta 8380

accactgcgg tcaaaccact tgcccacaaa accactaatg gcaccccggg gaatacctgc 8440

ataagtaggt gggcgggcca agataggggc gcgattgctg cgatctggag gacaaattac 8500
```

Figure 13N

```
acacacttgc gcctgagcgc caagcacagg gttgttggtc ctcatattca cgaggtcgct 8560

gagagcacgg tgggctaatg ttgccatggg tagcatatac tacccaaata tctggatagc 8620

atatgctatc ctaatctata tctgggtagc ataggctatc ctaatctata tctgggtagc 8680

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ctttgcatat gccgccacct cccaaggggg cgtgaatttt cgctgcttgt ccttttcctg 9280
     oriP
catgctggtt gctcccattc ttaggtgaat ttaaggaggc caggctaaag ccgtcgcatg 9340
```

Figure 13O

tctgattgct caccaggtaa atgtcgctaa tgttttccaa cgcgagaagg tgttgagcgc 9400

ggagctgagt gacgtgacaa catgggtatg cccaattgcc ccatgttggg aggacgaaaa 9460

tggtgacaag acagatggcc agaaatacac caacagcacg catgatgtct actggggatt 9520

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gccattccaa aggggagacg actcaatggt gtaagacgac attgtggaat agcaagggca 9940

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acccaagttc cttcgtcggt agtcctttct acgtgactcc tagccaggag agctcttaaa 10060

ccttctgcaa tgttctcaaa tttcgggttg gaacctcctt gaccacgatg ctttccaaac 10120

caccctcctt ttttgcgcct gcctccatca ccctgacccc ggggtccagt gcttgggcct 10180

Figure 13P

tctcctgggt catctgcggg gccctgctct atcgctcccg ggggcacgtc aggctcacca 10240

tctgggccac cttcttggtg gtattcaaaa taatcggctt cccctacagg gtggaaaaat 10300

ggccttctac ctggaggggg cctgcgcggt ggagacccgg atgatgatga ctgactactg 10360

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Figure 13Q

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ggattctcgg gacccctcct cttcctcttc aaggtcacca gacagagatg ctactggggc 11860

```
Figure 13R                                        ClaI
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atgataataa tggtttctta gacgtcaggt ggcacttttc ggggaaatgt gcgcggaacc 12040

cctatttgtt tatttttcta aatacattca aatatgtatc cgctcatgag acaataaccc 12100

tgataaatgc ttcaataata ttgaaaaagg aagagtatga gtattcaaca tttccgtgtc 12160

gcccttattc ccttttttgc ggcattttgc cttcctgttt ttgctcaccc agaaacgctg 12220

gtgaaagtaa aagatgctga agatcagttg ggtgcacgag tgggttacat cgaactggat 12280

ctcaacagcg gtaagatcct tgagagtttt cgccccgaag aacgttttcc aatgatgagc 12340

acttttaaag ttctgctatg tggcgcggta ttatcccgtg ttgacgccgg gcaagagcaa 12400

ctcggtcgcc gcatacacta ttctcagaat gacttggttg agtactcacc agtcacagaa 12460

aagcatctta cggatggcat gacagtaaga gaattatgca gtgctgccat aaccatgagt 12520
                                         PvuI
gataacactg cggccaactt acttctgaca acgatcggag gaccgaagga gctaaccgct 12580

tttttgcaca acatggggga tcatgtaact cgccttgatc gttgggaacc ggagctgaat 12640

gaagccatac caaacgacga gcgtgacacc acgatgcctg cagcaatggc aacaacgttg 12700
```

Figure 13S

cgcaaactat taactggcga actacttact ctagcttccc ggcaacaatt aatagactgg 12760

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attgctgata aatctggagc cggtgagcgt gggtctcgcg gtatcattgc agcactgggg 12880

ccagatggta agccctcccg tatcgtagtt atctacacga cggggagtca ggcaactatg 12940

gatgaacgaa atagacagat cgctgagata ggtgcctcac tgattaagca ttggtaactg 13000

tcagaccaag tttactcata tatactttag attgatttaa aacttcattt ttaatttaaa 13060

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ataccaaata ctgtccttct agtgtagccg tagttaggcc accacttcaa gaactctgta 13360

gcaccgccta catacctcgc tctgctaatc ctgttaccag tggctgctgc cagtggcgat 13420

aagtcgtgtc ttaccgggtt ggactcaaga cgatagttac cggataaggc gcagcggtcg 13480

ggctgaacgg ggggttcgtg cacacagccc agcttggagc gaacgaccta caccgaactg 13540

Figure 13T

agatacctac agcgtgagct atgagaaagc gccacgcttc ccgaagggag aaaggcggac 13600

aggtatccgg taagcggcag ggtcggaaca ggagagcgca cgagggagct tccaggggga 13660

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NruI

ggaagcgaga agaatcataa tggggaaggc catccagcct cgcgtcgcga acgccagcaa 14260

gacgtagccc agcgcgtcgg ccgccatgcc ctgcttcatc cccgtggccc gttgctcgcg 14320

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Figure 13U

```
aaccccgccc agcgtcttgt cattggcgaa ttcgaacacg cagatgcagt cggggcggcg 14440

cggtcccagg tccacttcgc atattaaggt gacgcgtgtg gcctcgaaca ccgagcgacc 14500

ctgcagcgac ccgcttaaca gcgtcaacag cgtgccgcag atcccgggca atgagatatg 14560

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cggtcaatac actacatggc gtgatttcat atgcgcgatt gctgatcccc atgtgtatca 15040

ctggcaaact gtgatggacg acaccgtcag tgcgtccgtc gcgcaggctc tcgatgagct 15100

gatgctttgg gccgaggact gccccgaagt ccggcacctc gtgcacgcgg atttcggctc 15160

caacaatgtc ctgacggaca atggccgcat aacagcggtc attgactgga gcgaggcgat 15220
```

Figure 13V

gttcggggat tcccaatacg aggtcgccaa catcttcttc tggaggccgt ggttggcggg 15280

tatggagcag cagacgcgct acttcgagcg gaggcatccg gagcttgcag gatcgccgcg 15340

gctccgggcg tatatgctcc gcattggtct tgaccaactc tatcagagct tggttgacgg 15400

caatttcgat gatgcagctt gggcgcaggg tcgatgcgac gcaatcgtcc gatccggagc 15460

cgggactgtc gggcgtacac aaatcgcccg cagaagcgcg gccgtctgga ccgatggctg 15520

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ggagacaata ccggaaggaa cccgcgctat gacggcaata aaaagacaga ataaaacgca 15640

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agacccatgg tttttggatg gcctgggcat ggaccgcatg tactggcgcg acacgaacac 16000

cgggcgtctg tggctgccaa acaccccccga cccccaaaaa ccaccgcgcg gatttctggc 16060

Figure 13W

```
           SalI
gtgccaagct agtcgaccaa                                   16080
```

CTGTTGGGCTCGCGGTTGAGGACAAACTCTTCGCGGTCTTTCCAGTACTCTTGGATCGGAAAC
CCGTCGGCCTCCGAACGGTACTCCGCCACCGAGGGACCTGAGCGAGTCCGCATCGACCGGAT
CGGAAAACCTCTCGACTGTTGGGGTGAGTACTCCCTCTCAAAAGCGGGCATGACTTCTGCGCT
AAGATTGTCAGTTTCCAAAAACGAGGAGGATTTGATATTCACCTGGCCCGCGGTGATGCCTTT
GAGGGTGGCCGCGTCCATCTGGTCAGAAAAGACAATCTTTTTGTTGTCAAGCTTGAGGTGTGG
CAGGCTTGAGATCTGGCCATACACTTGAGTGACAATGACATCCACTTTGCCTTTCTCTCCACAG
GTGTCCACTCCCAGGTCCAACTGCAGGTCGACTCTAGACCC

FIG. 14A

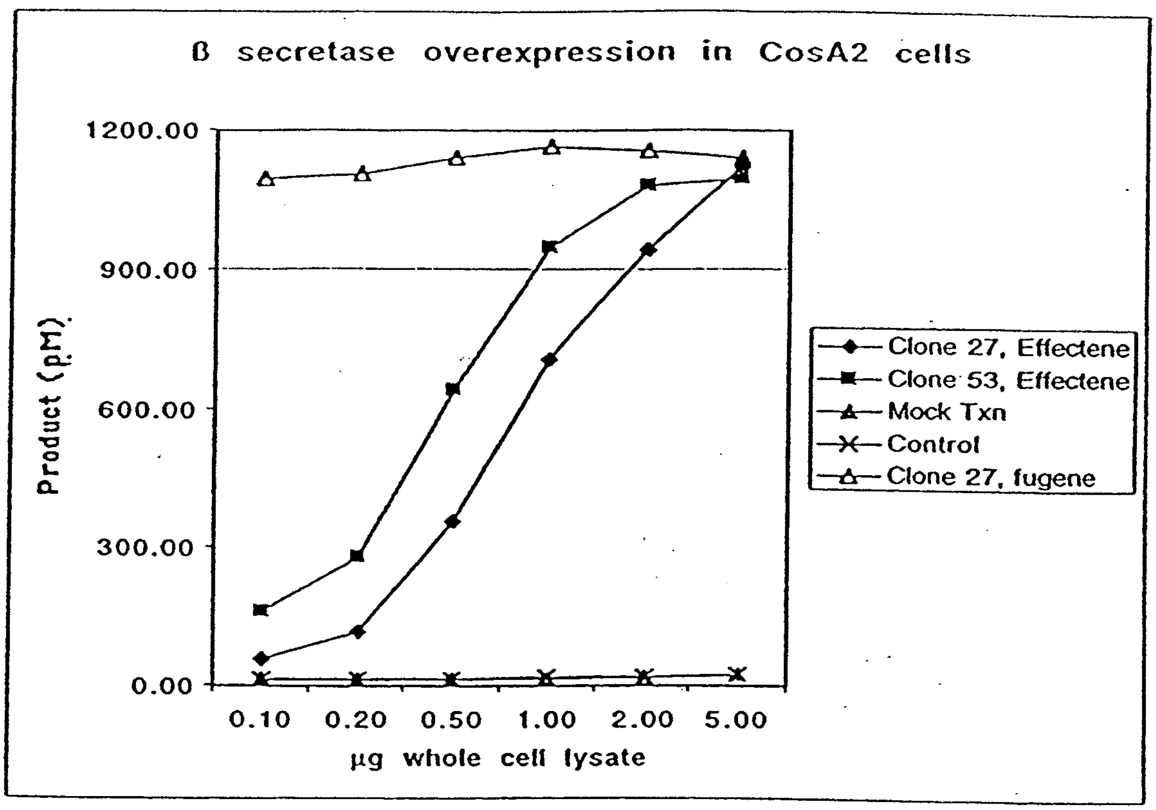

FIG. 14B

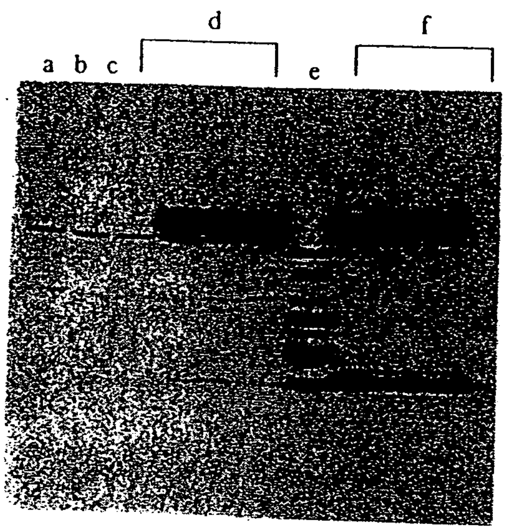

FIG. 15A

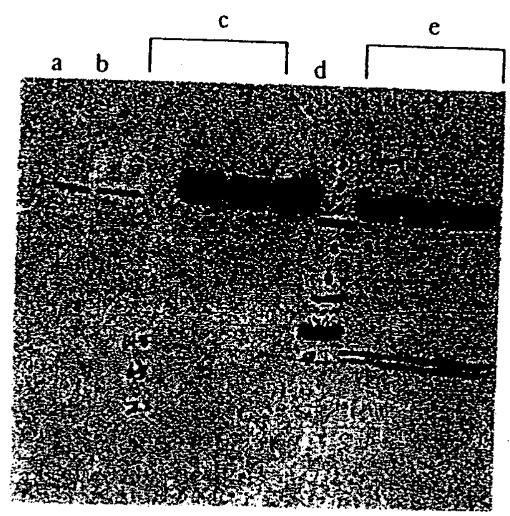

FIG. 15B

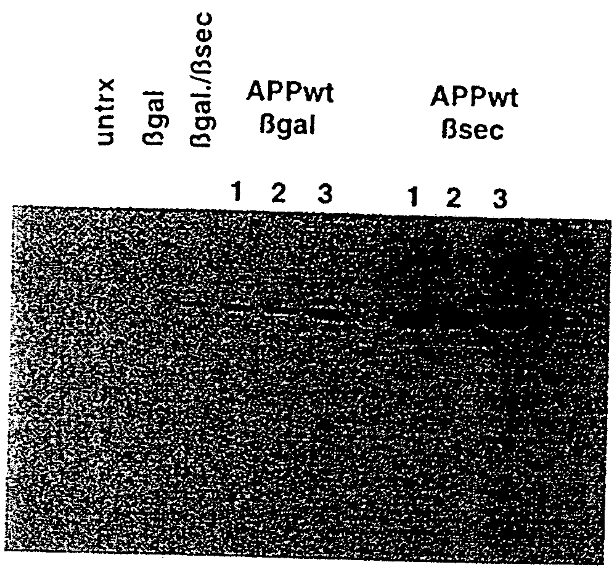

FIG. 16A

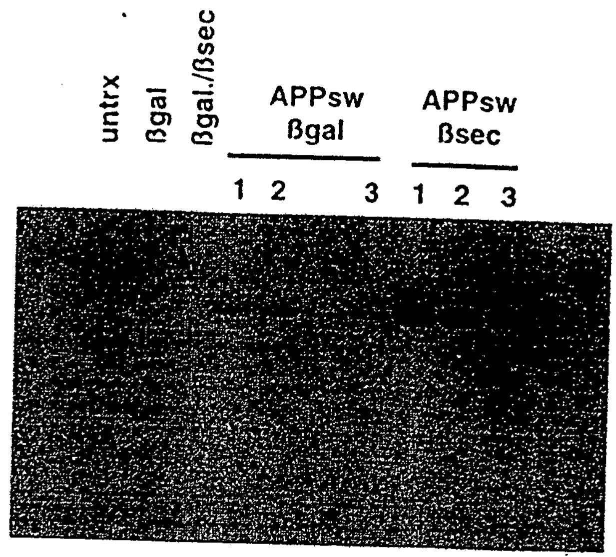

FIG. 16B

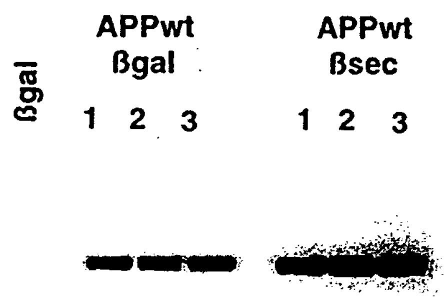

FIG. 17A

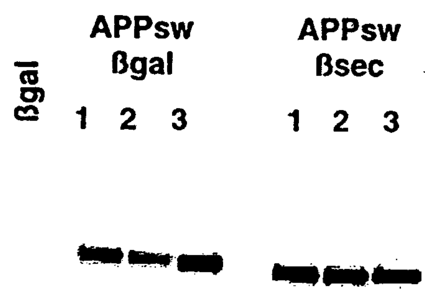

FIG. 17B

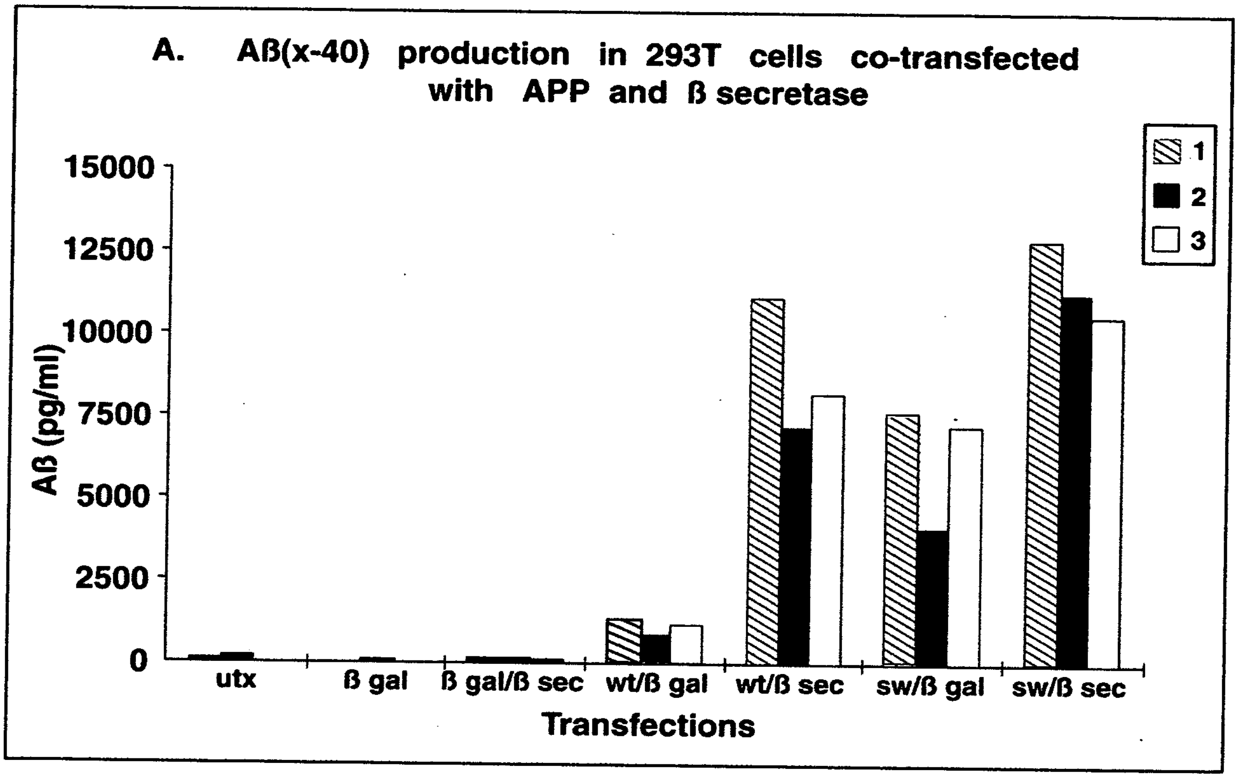
A. Aß(x-40) production in 293T cells co-transfected with APP and ß secretase
1
2
3
15000
12500
10000
7500
5000
2500
0
Aß (pg/ml)
utx
ß gal
ß gal/ß sec
wt/ß gal
wt/ß sec
sw/ß gal
sw/ß sec
Transfections

Fig. 18

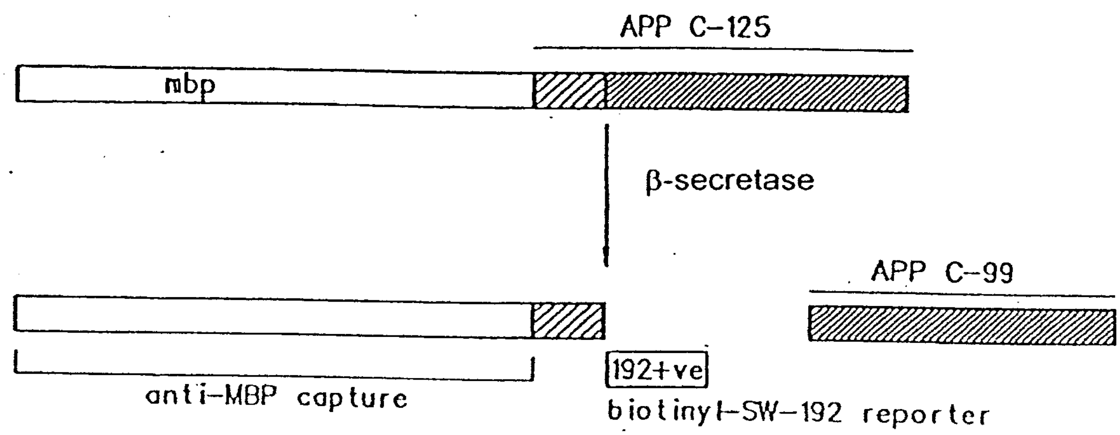

FIG. 19A

Wild-Type Sequence	....Val-Lys-Met-Asp...
Swedish Sequence	....Val-Asn-Leu-Asp...

FIG. 19B

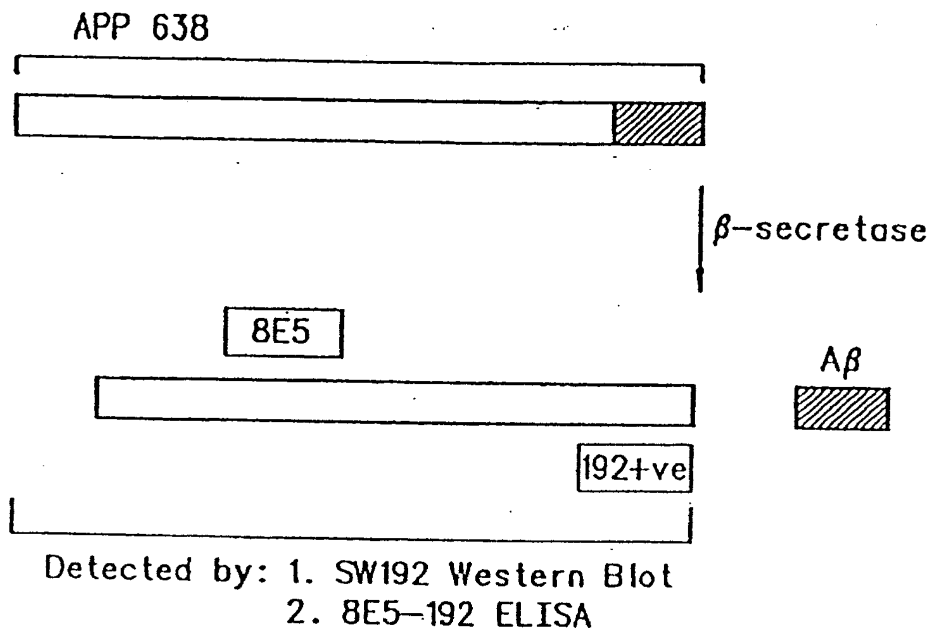
APP 638
β–secretase
8E5
Aβ
192+ve
Detected by: 1. SW192 Western Blot
2. 8E5–192 ELISA

FIG. 20

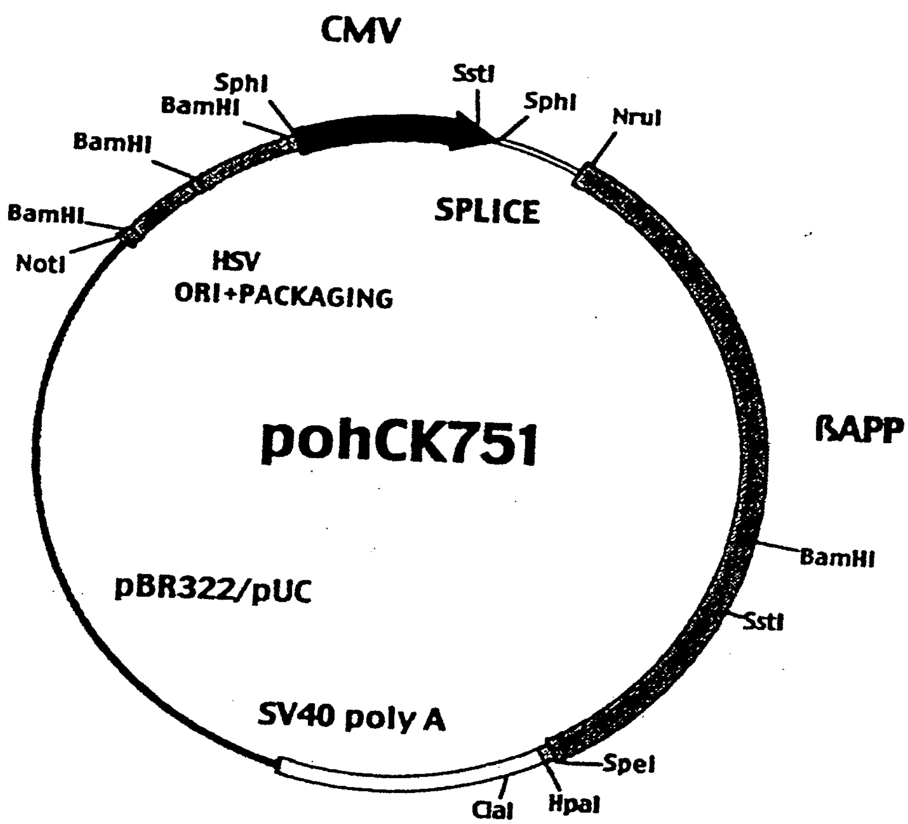
CMV
SphI
BamHI
SstI
SphI
NruI
BamHI
BamHI
NotI
SPLICE
HSV
ORI+PACKAGING
pohCK751
ßAPP
BamHI
pBR322/pUC
SstI
SV40 poly A
SpeI
ClaI
HpaI

FIG. 21